this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Specification:

Please replace the paragraph beginning on page 1, line 10 with the following two paragraphs:

This application is a continuation in part of U.S. Appl. No. 09/189,702, (134.10) filed November 10, 1998; which is a continuation in part U.S. Appl. No. 08/347,610, (50.50) filed December 1, 1994; and is a continuation in part of U.S. Application No. 08/205,713, (58.30) filed March 4, 1994; said U.S. Appl. No. 08/347,610 (50.50) is a continuation in part of U.S. Appl. No. 08/159,339, (50.30) filed November 29, 1993, U.S. Patent No. 6,037,135; which is a continuation in part of U.S. Appl. No. 08/103,396, (50.20) filed August 6, 1993, abandoned; which is a continuation in part of U.S. Appl. No. 08/027,746, (50.10) filed March 5, 1993, abandoned; which is a continuation in part of U.S. Appl. No. 07/926,666, (50.00) filed August 7, 1992, abandoned; said U.S. Appl. No. 08/205,713 (58.30) is a continuation in part of U.S. Appl. No. 08/159,184, (58.20) filed November 29, 1993, abandoned; which is a continuation in part of U.S. Appl. No.08/073,205, (58.10) filed June 4, 1993, abandoned; which is a continuation in part of U.S. Appl. No. 08/027,146, (58.00) filed March 5, 1993, abandoned.

The present application is also related to U.S.S.N. 09/226,775, which is a CIP of abandoned U.S.S.N. 08/815,396, which claims benefit of abandoned U.S.S.N. 60/013,113. Furthermore, the present application is related to U.S.S.N. 09/017,735, which is a CIP of abandoned U.S.S.N. 08/589,108; U.S.S.N. 08/454,033; and U.S.S.N. 08/349,177. The present application is also related to U.S.S.N. 09/017,524, U.S.S.N. 08/821,739, which claims benefit of abandoned U.S.S.N. 60/013,833; and U.S.S.N. 08/347,610, which is a CIP of U.S.S.N. 08/159,339, which is a CIP of abandoned U.S.S.N. 08/103,396, which is a CIP of abandoned U.S.S.N. 08/027,746, which is a CIP of abandoned U.S.S.N. 07/926,666. The present application is also related to U.S.S.N. 09/017,743, which is a CIP of abandoned U.S.S.N. 08/590,298; and U.S.S.N. 08/452,843, which is a CIP of U.S.S.N. 08/344,824, which is a CIP of abandoned U.S.S.N. 08/278,634. The present application is also related to PCT application 99/12066 filed 5/28/99 which claims benefit of provisional U.S.S.N. 60/087,192; U.S.S.N. 09/009,953, which is a CIP of abandoned U.S.S.N. 60/036,713; and abandoned U.S.S.N. 60/037,432. In addition, the present application is related to U.S.S.N. 09/098,584; U.S.S.N. 09/239,043; U.S.S.N. 60/117,486; U.S.S.N. 09/350,401; U.S.S.N. 09/357,737; and U.S.S.N. 09/390,061. All of the above applications in this paragraph are incorporated herein by reference.

Please replace the paragraph beginning on page 1, line 35, following the Statement Regarding Federally Sponsored Research or Development in the amendment submitted April 27, 2001 with the following paragraph in accordance with 37 C.F.R. § 1.52(e)(5):

The Sequence Listing written in file 115490_1, 2,346,548 bytes, created on March 24, 2003 on two identical copies of compact discs for Application No. 09/412,863, Sette *et*

al., Inducing Cellular Immune Responses to Human Immunodeficiency Virus-1 Using Peptide and Nucleic Acid Compositions, is herein incorporated-by-reference.

Please replace the paragraph beginning on page 12, line 13 with the following paragraph:

The term "peptide" is used interchangeably with "oligopeptide" in the present specification to designate a series of residues, typically L-amino acids, connected one to the other, typically by peptide bonds between the α-amino and carboxyl groups of adjacent amino acids. The preferred CTL-inducing peptides of the invention are less than 15 residues in length or 13 residues or less in length and usually consist of between about 8 and about 11 residues, preferably 9 or 10 residues. The preferred HTL-inducing oligopeptides are less than about 50 residues in length and usually consist of between about 6 and about 30 residues, more usually between about 12 and 25, and often between about 15 and 20 residues.

Please replace the paragraph beginning on page 44, line 13 with the following paragraph:

In some instances it may be desirable to combine the class I peptide vaccines of the invention with vaccines which induce or facilitate neutralizing antibody responses to the target antigen of interest, particularly to viral envelope antigens. A preferred embodiment of such a composition comprises class I and class II epitopes in accordance with the invention. An alternative embodiment of such a composition comprises a class I and/or

class II epitope in accordance with the invention, along with a PADRE® (Epimmune, San Diego, CA) molecule (described, for example, in U.S. Patent Number 5,736,142). Furthermore, any of these embodiments can be administered as a nucleic acid mediated modality.

Please replace the paragraph beginning on page 47, line 11 with the following paragraph:

A growing body of experimental evidence demonstrates that a number of different approaches are available which allow simultaneous delivery of multiple epitopes. Nucleic acids encoding the peptides of the invention are a particularly useful embodiment of the invention. Epitopes for inclusion in a minigene are preferably selected according to the guidelines set forth in the previous section. A preferred means of administering nucleic acids encoding the peptides of the invention uses minigene constructs encoding a peptide comprising one or multiple epitopes of the invention. The use of multi-epitope minigenes is described below and in, *e.g.*, co-pending application U.S.S.N. 09/311,784; Ishioka *et al.*, *J. Immunol.* 162:3915-3925, 1999; An, L. and Whitton, J. L., *J. Virol.* 71:2292, 1997; Thomson, S. A. *et al.*, *J. Immunol.* 157:822, 1996; Whitton, J. L. *et al.*, *J. Virol.* 67:348, 1993; Hanke, R. *et al.*, *Vaccine* 16:426, 1998. For example, a multi-epitope DNA plasmid encoding nine dominant HLA-A*0201- and A11-restricted epitopes derived from the polymerase, envelope, and core proteins of HBV and human immunodeficiency virus (HIV), the PADRE® universal helper T cell (HTL) epitope, and an endoplasmic reticulum-translocating signal sequence was engineered. Immunization of HLA transgenic mice with this plasmid construct resulted in strong CTL induction responses against the nine epitopes

tested, similar to those observed with a lipopeptide of known immunogenicity in humans, and significantly greater than immunization in oil-based adjuvants. Moreover, the immunogenicity of DNA-encoded epitopes *in vivo* correlated with the *in vitro* responses of specific CTL lines against target cells transfected with the DNA plasmid. Thus, these data show that the minigene served to both: 1.) generate a CTL response and 2.) that the induced CTLs recognized cells expressing the encoded epitopes. A similar approach may be used to develop minigenes encoding HIV epitopes.

Please replace the paragraph beginning on page 49, line 12 with the following paragraph:

In some embodiments, a bi-cistronic expression vector which allows production of both the minigene-encoded epitopes and a second protein (included to enhance or decrease immunogenicity) can be used. Examples of proteins or polypeptides that could beneficially enhance the immune response if co-expressed include cytokines (*e.g.*, IL-2, IL-12, GM-CSF), cytokine-inducing molecules (*e.g.*, LeIF), costimulatory molecules, or for HTL responses, pan-DR binding proteins (PADRE®, Epimmune, San Diego, CA). Helper (HTL) epitopes can be joined to intracellular targeting signals and expressed separately from expressed CTL epitopes; this allows direction of the HTL epitopes to a cell compartment different than that of the CTL epitopes. If required, this could facilitate more efficient entry of HTL epitopes into the HLA class II pathway, thereby improving HTL induction. In contrast to HTL or CTL induction, specifically decreasing the immune response by co-expression of immunosuppressive molecules (*e.g.* TGF-β) may be beneficial in certain diseases.

Please replace the paragraph beginning on page 52, line 7 with the following paragraph:

Alternatively, it is possible to prepare synthetic peptides capable of stimulating T helper lymphocytes, in a loosely HLA-restricted fashion, using amino acid sequences not found in nature (*see, e.g.*, PCT publication WO 95/07707). These synthetic compounds called Pan-DR-binding epitopes (*e.g.*, PADRE®, Epimmune, Inc., San Diego, CA) are designed to most preferrably bind most HLA-DR (human HLA class II) molecules. For instance, a pan-DR-binding epitope peptide having the formula: aKXVWANTLKAAa, (SEQ ID NO:14491) where "X" is either cyclohexylalanine, phenylalanine, or tyrosine, and a is either D-alanine or L-alanine, has been found to bind to most HLA-DR alleles, and to stimulate the response of T helper lymphocytes from most individuals, regardless of their HLA type. An alternative of a pan-DR binding epitope comprises all "L" natural amino acids and can be provided in the form of nucleic acids that encode the epitope.